Occupation and pancreatic cancer in Spain: a case-control study based on job titles

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Background	Occupational exposures may increase the risk of exocrine pancreatic cancer. This study aimed to identify occupations that in Spain may be associated with such risk.
Methods	Incident cases of pancreatic cancer and hospital controls were prospectively identified and interviewed during their hospital stay. Occupational history was obtained by direct interview with the patient and was available for 164 (89%) of 185 pancreatic cancer cases and for 238 (90%) of 264 controls. Occupations were coded according to the Spanish version of the International Standard Classification of Occupations 1988.
Results	A significant increased odds ratio (OR) was observed in men for 'physical, chemistry and engineering science technicians'. Elevated risks were also found for 'metal moulders, sheet-metal workers, structural metal workers, welders and related workers', 'painters and varnishers' and 'machinery mechanics and fitters'. 'Agricultural workers' did not present an increased risk for pancreas cancer in men. In women, however, high OR were observed for 'agricultural workers' and for 'textile and garment workers'. Most associations remained unchanged after considering long duration of the exposure and the period 5–15 years before diagnosis.
Conclusions	Few occupations were at increased risk for pancreatic cancer, and the associations observed are in accordance with previous studies. The increases in risk observed for women in agricultural and textile jobs, and for men in the manufacture of dyes and pigments may deserve further attention.
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Pancreatic cancer is a highly lethal malignancy whose aetiology is largely unknown. The only firmly established and modifiable risk factor is smoking, but it explains only a fraction of cases,[1] and the association seems somewhat weaker in Mediterranean countries.[2,3] A recent meta-analysis on occupation has concluded that occupational exposures may increase the risk of exocrine pancreatic cancer.[4] However, studies have often been negative, and no single occupation has consistently been shown to increase the risk of this malignancy.[1,4–9] Because of the clinical aggressiveness of the disease, many occupational studies have been based on deceased cases; this fact limits the quality of the information available for cases and constrains the selection of controls. On the other hand, studies on pancreatic cancer relying on personal interviews[10–12] have achieved response rates of 40–60%. In spite of these and other limitations, an increased risk has been observed among

workers manufacturing DDT (dichlorodiphenyltrichloroethane)[13] and, to a lesser extent, among those agricultural workers applying pesticides.[6,14–24] Additional increases in the risk have also been seen in dry cleaning,[9] the chemical industry,[25,26] leather tanning,[27,28] printing,[24,29] petrol derivatives,[24,30,31] mechanics,[32,33] metal industry,[23,34–37] and textile industry workers.[6,23,28,32,38,39] The recent meta-analysis[4] found significantly increased risks for chlorinated hydrocarbon solvents and for nickel compounds, and non-statistically significant risks for chromium compounds, polycyclic aromatic hydrocarbons, organochlorine insecticides, silica dust, and aliphatic and alicyclic hydrocarbon solvents.[4] The proportion of cases of pancreas cancer explained by occupational exposures has been reported to be 1%,[40] 12%[4] and 26%.[24]

In Spain, uncertainties surrounding occupational cancers are especially large, since few studies exist; none is available for pancreatic cancer.[41] Although this neoplasm does not represent one of the major causes of cancer mortality in Spain, its mortality has increased dramatically over the last 40 years, showing the steepest upward trend of all Europe.[42] It is unknown to what extent such an increase is related to the accuracy of death certification, changes in lifestyle or other environmental factors.[42,43]

The purpose of the present study was to identify occupations that, in Spain, may be associated with an increased risk of pancreatic cancer.

Material and Methods

Subjects

Methods have been described in detail elsewhere.[44–49] Briefly, subject recruitment took place in 1992–1995 at five general hospitals in eastern Spain. Incident cases of pancreatic cancer (n = 185) and hospital controls (n = 264) were prospectively identified and interviewed during hospital stay. Controls were subjects free of pancreatic cancer who had been admitted to the same hospitals with an initial diagnostic suspicion of pancreatic cancer, biliary cancer or chronic pancreatitis. At the end of recruitment, a panel of experts in pancreatic cancer reviewed the primary diagnoses of all patients on the basis of all clinical and pathological information available, including follow-up.[45,49] Occupational histories were obtained for 164 (88.6%) cases and for 238 (90.2%) controls. Referents included 93 patients with chronic pancreatitis, 34 with acute pancreatitis, 41 with other cancers and 70 individuals with other benign pathologies, mainly biliary pathology.

Trained monitors conducted interviews with patients during the hospital stay. The questions concerned clinical history, symptoms preceding admission, occupation and lifestyle. Most interviews were conducted with the patient (88% with the patient alone and 6% with the patient plus a relative). To assess the reliability of responses, a sample of 110 relatives was concurrently and separately interviewed, and high agreement between the two sets of responses was found.[44] The study protocol was approved by the Ethics Committee of the participating hospitals, and patients gave their informed consent prior to their inclusion in the study.

Occupational exposures

Patients were asked if they had ever worked in any of ten activities a priori defined as potentially related to pancreas and biliary cancers, according to a review of the literature. These were pesticide use, handling of petroleum derivatives, the chemical industry, the metal industry, rubber industry, graphic arts, jewellery, manufacture or repair of automobiles, leather tanning, and the textile industry. When the patient reported having worked in any of such activities, he/she was asked for the duration of exposure, particular activity, and products to which he/she had been exposed. In addition, they were asked about any other activity performed for at least 6 years. The occupations obtained were coded according to the Spanish National Classification of Occupations 1994 (CNO94), which is adapted from the International Standard Classification of Occupations 1988.

Statistical analysis

The risk for pancreatic cancer was estimated for any occupation held for at least one year. Job titles were initially examined based on one-digit major occupational groups and two-digit subcategories. Risks for the a priori high-risk occupations were further assessed by duration of exposure and by applying a period analysis.

Univariate statistics were computed as customary.[44–51] Odds ratios (OR) were calculated to estimate the magnitude of associations between each occupational exposure and pancreatic cancer. The associations were explored separately for men and women. Multivariate-adjusted OR and 95% CI were estimated by unconditional logistic regression. The following potential confounders were included in the models: age (quartiles), hospital, smoking (five categories: non-smoker and quartiles for pack-years), coffee consumption (number of weekly cups during the year prior to the first symptom), and alcohol use (non-drinker, occasional, low consumption, high consumption and heavy drinker).[52] Allowance for other potential confounding variables (e.g. schooling, diabetes) did not substantially modify any of the estimates. If the observed number of people in one cell of the contingency table was zero, the Woolf-Haldane correction was applied.[53] The level of statistical significance was set at 0.05 and all tests were two-tailed.

Results

There were no differences in the distribution of age, gender and study centre between patients who provided occupational information and those who did not. Main characteristics of cases and controls are shown in Table 1. Pancreatic cancer cases were on average about 5 years older than controls in both men and women. Differences between cases and controls in years of education, and tobacco, alcohol and coffee consumption were not statistically significant. In particular, heavy alcohol drinkers were more frequent among controls, due to the presence of subjects with pancreatitis. These differences will be accounted for through multivariate analysis.

The median number of occupations reported by men and women was two and one, respectively ($P < 0.01$). Among men, almost 40% of pancreatic cancer cases reported having worked as 'skilled workers' (10% in women), one-third of patients had worked as 'machinery operators' (25% in women), and one-third as agricultural workers (25% in women). Among women almost one-third of cases were exclusively housewives (18% among controls) (data not shown).

Table 1 Socio-demographic and lifestyle characteristics of cases and controls

	Men			Women		
	Cases/controls	Odds ratio[a]	(95% CI)	Cases/controls	Odds ratio[a]	(95% CI)
No. of subjects	96/167			68/71		
Age (years)						
Mean (SD)	63.3 (11.4)/58.0 (15.0)			71.8 (12.3)/67.9 (14.0)		
35–54	21/78	1.0		5/13	1.0	
55–66	34/31	4.1	(2.1–8.0)	16/17	2.4	(0.7–8.4)
67–74	26/36	2.7	(1.3–5.3)	15/17	2.3	(0.7–7.9)
≥75	15/22	2.5	(1.1–5.7)	32/24	3.5	(1.1–11.0)
Education						
Illiterate	7/12	1.0		12/17	1.0	
Able only to read and write	23/29	0.5	(0.1–2.0)	20/17	1.6	(0.5–5.0)
≤10 years of schooling	54/99	1.0	(0.3–3.4)	31/32	2.0	(0.7–5.2)
Schooling for >10 years	11/26	0.6	(0.1–2.3)	4/2	12.7	(0.9–189)
Smoking						
Never	11/14	1.0		61/63	1.0	
Ever	85/152	1.0	(0.4–2.6)	7/8	1.4	(0.4–5.2)
1–25 pack-years	24/29	1.4	(0.4–4.1)	3/5	1.2	(0.2–6.8)
26–40 pack-years	21/42	1.0	(0.3–3.2)	4/3[b]	1.7	(0.3–9.8)
41–60 pack-years	20/48	0.6	(0.2–1.8)	–		
>60 pack-years	20/33	1.2	(0.4–3.9)	–		
Alcohol						
Non-drinker	3/2	1.0		21/28	1.0	
Occasional drinker	8/1	1.0	(0.0–24.8)	11/9	0.7	(0.2–2.7)
Low consumption	29/26	0.6	(0.1–5.2)	25/22	1.2	(0.5–3.0)
High consumption	25/37	0.4	(0.0–4.2)	6/6	1.6	(0.4–6.1)
Heavy drinker	31/100	0.2	(0.2–2.0)	5/6	0.6	(0.1–2.9)
Coffee						
Non-regular drinkers	83/151	1.0		57/58	1.0	
Regular coffee drinkers	13/15	0.9	(0.3–2.4)	11/12	0.7	(0.2–2.2)

[a] Adjusted for age and where appropriate, hospital, education and consumption of alcohol, tobacco, and coffee.

[b] >26 pack-years.

Table 2 shows the risk estimators for pancreatic cancer according to gender for all major occupational groups (one-digit), and for subgroups (two-digit) with at least four exposed subjects. In men, a 2.6-fold increase in risk of pancreatic cancer was found for 'general managers and government administrators'. This association was stronger within the subgroup 'working proprietors (wholesale and retail trade)' (OR = 12, 95% CI : 0.9–157). For the major group 'support technicians and professionals' an OR of 2.1 was observed (95% CI : 0.7–6.0), which rose to 20 (95% CI : 1.8–228) within the subgroup of 'physical, chemistry and engineering science technicians', the only subgroup whose increase in risk was statistically significant. Non-significant twofold increased risks were found for 'support professionals in financial and commercial operations', 'supervisor of stationary machinery operators', and 'machinery fitters and machine assemblers'. Slight increases were observed among 'skilled workers in agricultural activities', 'unskilled workers in agriculture and fishing', and 'unskilled construction workers'. In women, OR were elevated in 'skilled workers in agricultural activities' (OR = 2.2, 95% CI : 0.8–6.2) and 'unskilled manufacturing industry workers' (OR = 4.2, 95% CI : 0.6–29) (Table 2).

When patients with pancreatitis were excluded from the control group, the associations found for men tended to decrease slightly; the exceptions being 'general managers and government administrators' (OR = 4.7, 95% CI : 0.9–25), 'finishing building workers' (OR = 6.0, 95% CI : 0.6–60), 'sheet-metal workers, blacksmiths, welders, structural metal workers, toolmakers, machine-tool setter-operators, and related workers' (OR = 3.3, 95% CI : 0.5–21). In women the OR increased slightly in agricultural workers.

Results by duration of employment are shown in Table 3. In men, the association observed for 'physical, chemistry and engineering science technicians' remained unchanged (all exposed subjects had worked for at least 20 years). Job titles associated with a higher socioeconomic status ('general managers and government administrators' and 'trade agents') showed increased OR when considering long duration of the activity. The same pattern was apparent for construction-related occupations ('structural building workers', 'construction machinery operators', and 'unskilled construction workers'), and among 'painters', 'supervisors of stationary machinery operators', and 'machinery mechanics and fitters'. High increases in risk were found when working less than 20 years as

Table 2 Risk estimates for pancreatic cancer for major (one-digit) and subgroup (two-digit) occupational subcategories, by gender[a]

CNO94[b] codes and job titles[c]	Men Cases/controls[d] (96/167)	Odds ratio[e]	(95% CI)	Women Cases/controls[d] (68/71)	OR[e]	(95% CI)
1. General managers and government administrators	9/9	2.6	(0.8–8.2)	2/1	2.4	(0.2–30)
15. Working proprietor (wholesale and retail trade)	4/1	11.8	(0.9–157)	1/1	1.1	(0.1–20)
2. Scientific professionals and technicians	2/5	0.4	(0.1–2.9)	2/1	4.5	(0.4–58)
3. Support technicians and professionals	10/11	2.1	(0.7–6.0)	0/0	–	
30. Physical, chemistry and engineering science technicians	4/1	20.2	(1.8–228)	0/0	–	
33. Support professionals in financial and commercial operations	4/5	2.0	(0.4–10)	0/0	–	
4. Clerical and related workers	6/17	0.6	(0.2–1.9)	2/0	5.2[f]	(0.2–111)
5. Catering and hospitality, personal, and security services workers, and salesmen	13/28	0.8	(0.3–2.0)	8/9	1.7	(0.5–5.5)
50. Cooks, waiters, bartenders and related workers	5/12	0.7	(0.2–2.8)	2/1	3.0	(0.2–42)
53. Shop assistants and related workers	4/12	0.8	(0.2–3.3)	3/4	1.1	(0.2–6.3)
6. Skilled workers in agriculture and fishing	31/41	1.4	(0.7–2.6)	15/7	2.4	(0.9–6.8)
60. Skilled workers in agricultural activities	29/39	1.3	(0.6–2.5)	14/7	2.2	(0.8–6.2)
7. Craftsmen and skilled workers in manufacturing, construction, and mining, except installation and machinery operators	37/69	0.9	(0.5–1.7)	7/11	0.7	(0.2–2.2)
71. Structural building workers	12/16	1.1	(0.4–3.0)	0/0	–	
72. Finishing building workers	6/16	0.9	(0.3–2.7)	0/1	–	
75. Sheet-metal workers, blacksmiths, welders, structural metal workers, toolmakers, machine-tool setter-operators, and related workers	9/16	1.2	(0.4–3.3)	0/0	–	
76. Mechanics and fitters	6/12	1.1	(0.3–3.5)	0/0	–	
79. Wood treatment, cabinetmakers, textile workers, tailors and dressmakers, leather workers, shoemakers and related workers	4/9	0.9	(0.2–3.9)	5/9	0.7	(0.2–2.6)
8. Installation and machinery operators, and machine assemblers	32/72	0.8	(0.4–1.5)	18/21	0.8	(0.4–1.8)
82. Supervisor of stationary machinery operators	5/3	2.2	(0.5–10)	0/0	–	
83. Stationary machinery operators	17/30	0.9	(0.4–1.9)	16/20	0.7	(0.3–1.7)
84. Machinery fitters and machine assemblers	3/5	2.6	(0.5–13)	1/1	1.3	(0.1–24)
85. Mobile machine operators	4/9	1.0	(0.3–3.7)	1/0	–	
86. Motor vehicle drivers for urban or road transport	6/25	0.5	(0.2–1.5)	0/0	–	
9. Unskilled workers	26/52	1.1	(0.6–2.1)	49/53	0.8	(0.4–1.9)
91. Housekeeping service workers and other interior cleaning workers	0/1	–		42/49	0.6	(0.3–1.2)
94. Unskilled workers in agriculture and fishing	15/20	1.6	(0.7–3.7)	3/5	0.5	(0.1–2.7)
96. Unskilled construction workers	7/18	1.3	(0.5–4.0)	1/0	–	
97. Unskilled manufacturing industry workers	2/11	0.5	(0.1–2.7)	4/2	4.2	(0.6–29.2)

[a] Only for major groups and subgroups with more than four cases or controls.
[b] CNO94: Spain's National Classification of Occupations 1994 (adapted from ISCO 1988).
[c] One person can be included in more than one occupation.
[d] Number of exposed cases and controls.
[e] Adjusted for age, hospital, alcohol, coffee and tobacco.
[f] Crude OR, computed with the Woolf-Haldane correction.

Table 3 Risk estimates for pancreatic cancer of selected occupational subcategories, by years of working and by gender

CNO94[a] codes and job titles[b]	Years of working		
	0	<20	20+
Men			
1. General managers and government administrators			
Cases/controls	87/157	1/3	4/1
OR[c] (95% CI)	1	0.3 (0.0–4.3)	6.7 (0.6–78)
3. Support technicians and professionals			
Cases/controls	86/155	2/3	8/5
OR (95% CI)	1	1.2 (0.1–10.5)	3.2 (0.8–12)
30. Physical, chemistry and engineering science technicians			
Cases/controls	92/165	0/0	4/1
OR (95% CI)	1	–	20.2 (1.8–228)
3320. Trade agents			
Cases/controls	92/163	1/3	3/0
OR (95% CI)	1	0.9 (0.1–11.1)	12.4[d] (0.6–242)
601. Self-employed skilled workers in agricultural activities			
Cases/controls	72/133	11/19	12/13
OR (95% CI)	1	0.8 (0.3–2.1)	1.1 (0.4–3.1)
602. Employed skilled workers in agricultural activities			
Cases/controls	90/160	4/4	2/1
OR (95% CI)	1	2.5 (0.5–13.7)	2.9 (0.2–36.9)
71. Structural building workers			
Cases/controls	84/150	2/8	9/7
OR (95% CI)	1	0.4 (0.1–2.1)	1.7 (0.5–6.4)
7240. Painters, varnishers and related workers			
Cases/controls	93/158	0/7	3/1
OR (95% CI)	1	0.1[d] (0.0–2.0)	5.3 (0.5–61.2)
751. Metal moulders, sheet-metal workers, structural metal workers, welders and related workers			
Cases/controls	90/158	3/2	3/5
OR (95% CI)	1	8.8 (0.9–88)	1.4 (0.3–7.5)
76. Machinery mechanics and fitters			
Cases/controls	90/154	1/8	5/3
OR (95% CI)	1	0.3 (0.0–3.8)	3.4 (0.6–18.2)
82. Supervisor of stationary machinery operators			
Cases/controls	91/163	1/0	3/0
OR (95% CI)	1	–	12.5[d] (0.6–245)
8329. Machinery operators in the manufacture of dyes and pigments			
Cases/controls	93/166	2/0	1/0
OR (95% CI)	1	8.9[d] (0.4–187)	–
854. Construction machinery operators			
Cases/controls	91/157	0/2	3/1
OR (95% CI)	1	0.3[d] (0.0–7.20)	7.1 (0.6–80)
960. Unskilled construction workers			
Cases/controls	89/148	5/11	1/4
OR (95% CI)	1	1.6 (0.4–5.9)	1.5 (0.1–18)
Women			
601. Self-employed skilled workers in agricultural activities			
Cases/controls	54/65	4/0	8/5
OR (95% CI)	1	10.8[d] (0.6–205)	2.1 (0.6–7.6)
793. Textile and garment workers			
Cases/controls	63/63	0/7	5/1
OR (95% CI)	1	0.1[d] (0.0–1.2)	11.5 (1.0–135)

[a] CNO94: Spain's National Classification of Occupations 1994 (adapted from ISCO 1988).
[b] One person can be included in more than one occupation.
[c] Adjusted for age, hospital, alcohol, coffee and tobacco.
[d] Crude OR, computed with the Woolf-Haldane correction.

Table 4 Risk estimates for pancreatic cancer by time window before diagnosis and by gender

CNO94[a] codes and job titles[b]	Time window of exposure before diagnosis		
	No exposure	5–15 years	>15 years
Men			
1. General managers and government administrators			
Cases/controls	87/157	2/1	0/0
OR[c] (95% CI)	1	2.8 (0.1–5.7)	–
3. Support technicians and professionals			
Cases/controls	86/155	6/2	0/2
OR (95% CI)	1	7.3 (1.0–54)	0.4[d] (0.0–7.6)
30. Physical, chemistry and engineering science technicians			
Cases/controls	92/165	2/0	0/0
OR (95% CI)	1	8.9[d] (0.4–188)	–
3320. Trade agents			
Cases/controls	92/163	3/1	0/0
OR (95% CI)	1	3.3 (0.2–53)	–
601. Skilled workers in agricultural activities on own account			
Cases/controls	72/133	5/7	5/7
OR (95% CI)	1	0.7 (0.2–2.9)	0.9 (0.2–3.5)
602. Skilled workers in agricultural activities on other's account			
Cases/controls	90/160	1/2	1/1
OR (95% CI)	1	1.0 (0.1–15)	1.3 (0.0–56)
71. Structural building workers			
Cases/controls	84/150	8/5	1/2
OR (95% CI)	1	2.2 (0.5–10)	1.2 (0.0–2.4)
7240. Painters, varnishers and related workers			
Cases/controls	93/158	2/2	0/2
OR (95% CI)	1	1.6 (0.2–14)	0.3[d] (0.0–7.1)
751. Metal moulders, sheet-metal workers, structural metal workers, welders and related workers			
Cases/controls	90/158	3/3	2/1
OR (95% CI)	1	2.0 (0.3–12)	4.4 (0.2–8.1)
76. Machinery mechanics and fitters			
Cases/controls	90/154	2/1	0/3
OR (95% CI)	1	4.2 (0.2–70)	0.2[d] (0.0–4.8)
82. Supervisor of stationary machinery operators			
Cases/controls	91/163	2/0	1/0
OR (95% CI)	1	8.9[d] (0.4–188)	–
854. Construction machinery operators			
Cases/controls	91/157	3/0	0/1
OR (95% CI)	1	12.0[d] (0.6–236)	–
960. Unskilled construction workers			
Cases/controls	89/148	2/2	1/1
OR (95% CI)	1	5.3 (0.5–60)	0.4 (0.0–16)
Women			
601. Skilled workers in agricultural activities on own account			
Cases/controls	54/65	2/1	3/2
OR (95% CI)	1	2.0 (0.1–36)	1.5 (0.2–12)
793. Textile and garment workers			
Cases/controls	63/63	2/0	0/2
OR (95% CI)	1	5.0[d] (0.2–106)	0.2[d] (0.0–4.2)

[a] CNO94: Spain's National Classification of Occupations 1994 (adapted from ISCO 1988).

[b] One person can be included in more than one occupation.

[c] OR: Odds Ratio; CI: Confidence Interval. Adjusted for age, hospital, alcohol, coffee and tobacco.

[d] Crude OR, computed with the Woolf-Haldane correction.

'metal moulders, sheet-metal workers, structural metal workers, welders and related workers', or as 'machinery operators in the manufacture of dyes and pigments'. While 'self-employed skilled workers in agricultural activities' did not show any increase in risk, there were some indications of an association among those who performed their activity as employees. In women, increased OR were observed for any duration of exposure among 'skilled workers in agriculture' and only for longer than 20 years of duration in 'textile and garment work' (OR = 11, 95% CI : 1.0–135).

Table 4 shows the risk estimates by time period. Occupational activities that showed increased risk when considering long duration of exposure, were also found to be increased in the period 5–15 years before the diagnosis. However, all risk estimators tended to decrease slightly, except for 'machinery mechanics and fitters' (OR = 4.2, 95% CI : 0.2–12), 'construction machinery operators' (OR = 12, 95% CI : 0.6–236), and 'unskilled construction workers' (OR = 5.3, 95% CI : 0.5–60).

Discussion

Although most observed increases in risk were small and statistically non-significant, some associations must be highlighted: 'agricultural activities', and 'textile and garment workers' among women; and with 'physical and chemistry technicians', and 'manufacture of dyes and pigments', among men.

The increased risk of pancreatic cancer in agricultural workers was more consistent among women than among men, since among the latter an association was observed only among those who carried out their activity as employees but not among men who were self-employed. Lack of this association cannot be attributed to low statistical power, since the probability of detecting an OR of 2.5 among men was 90%.

Some authors have reported statistically significant risks of pancreatic cancer in agricultural and related occupations. In 1976 and in 1983, Milham[23] observed such risk among nurserymen in Washington. Alavanja et al.[14] found an OR of 2.2 in workers employed in flour mills. And in 1992, Garabrant et al.[13] reported a dose-response relationship in a cohort of workers manufacturing DDT. Later, several other studies have reported associations between pancreatic cancer and pesticide exposure,[6,15–17,19–22] although most lacked information about the specific type of pesticide used. Other studies found non-significant increases in the risk of pancreatic cancer in agricultural workers.[18,24] A recent meta-analysis[4] reported a meta-risk ratio of 1.5 (95% CI : 0.6–3.7) for organochlorine insecticides. A different meta-analysis evaluating cancer risk among farmers reported a slightly increased meta-relative risk for pancreatic cancer only when considering proportional mortality studies and case-control studies.[54] Several studies[55–60] among workers manufacturing pesticides did not find increased risks, although none had a substantial number of cases with histological confirmation. Diagnostic misclassification for pancreatic cancer has been shown to seriously bias risks.[13,61–66] The prospective identification of cases and the in-depth review of diagnoses performed in our study[45,49] greatly reduced the potential for diagnostic misclassification. Some epidemiological studies on pesticides may also have underestimated risks because of the difficulty of estimating cumulative personal exposure. Serum levels may provide accurate estimates of

individual internal dose for persistent compounds.[67,68] Thus, our findings on organochlorine compounds[46] may also deserve attention from an occupational perspective; we reported that cases of pancreatic cancer were more likely to have serum concentrations of p,p'-DDE than controls (multivariate-adjusted OR for upper versus lower tertile: 5.6 [95% CI : 1.3–24.6], P for trend 0.025).[46]

In agreement with other reports, the other important association found among women in our study was for textile workers.[6,23,28,32,38,39]

'Physical, chemistry and engineering science technicians', and 'machinery operators in the manufacture of dyes and pigments' showed the strongest associations among men in the present study. The latter group included workers potentially exposed to pigments and anilines. Some of these compounds are aromatic amines, known to be pancreatic carcinogens in animal models, and it has been suggested that they may play a role in human pancreatic cancer as well.[69] Mack et al.[5] also reported an RR above 2 (95% CI : 0.9–5.2) in workers handling dyes and, within a cohort of workers processing synthetic resins,[70] an OR of 7 (P < 0.05) was detected among those employed for more than 16 years in vinyl and polyethylene production. Furthermore, in a Finnish study,[6] a cluster of six cases (and no referents: indeterminate OR, P = 0.0004) was observed when pooling the similar branch categories 'synthetic resins, plastic materials and synthetic rubber' and 'plastic products not elsewhere classified'. Male and female Finnish hairdressers may also be at increased risk.[71]

We also observed an association with 'metal moulders and welders and related workers'. A recent case-control study in China[38] reported a threefold increased risk for pancreatic cancer among plumbers and welders. Similarly, Norell et al.[31] found an increased OR for pancreatic cancer in individuals exposed to welding materials, although not in welders. The association found among painters in our study could be due to exposure to some pigments or to solvents. Some studies[6,31] have seen an excess of pancreatic cancer among painters, whereas others have not.[72,73]

Weak associations were apparent for different job titles related to building construction. Other studies have reported increased risks among cement finishers,[6,74] bricklayers,[34] cranemen and derrickmen,[23,34,75] and construction workers.[38,76] Another association observed in the present study, although weak, concerns 'general managers'. Studies that made similar observations have invoked chance or methodological caveats,[6,28] since no explanation was forthcoming.

Occupations that showed an increased risk when considering long duration of exposure were also found to increase risk in the period 5–15 years before the diagnosis. This period is deemed critical in pancreatic carcinogenesis.[1,9–11,46]

The presence of heterogeneous exposures to agents in relatively broad occupational groups is another limitation of job title-based studies. Analyses based on an assessment of occupational histories by industrial hygienists are the subject of a separate report.[77]

Additional methodological issues should be considered in the interpretation of the results. Most pancreatitis is due to alcohol abuse or to obstruction of the pancreatic ducts.[78] Occupation plays a small or null role in the aetiology of the pathologies of controls,[77–81] more than half of whom suffered from chronic or

acute pancreatitis. The possibility that pancreatitis increases the risk of pancreas cancer or that the two entities share some risk factors,[1,9,82–84] would tend to mask the associations. However, after excluding from the referent group patients with pancreatitis, risk estimators were hardly modified. Also, the main results were adjusted for alcohol and smoking. The main advantages[85–87] of using subjects with other pathologies included in the PANKRAS II Study as a referent group are: (1) a decrease in potential interviewer bias, (2) economic efficiency, and (3) an increase in the specificity of the relationship between the exposure of interest and pancreatic cancer (versus other pancreatic diseases). Furthermore, because of the diagnostic suspicion criterion for entry into the study, all cases and referents followed a highly similar referral and diagnostic pathway; this maximized the likelihood that all subjects stemmed from a common study base. Other important case-control studies on pancreatic cancer and occupation used hospital controls,[32] cancer controls,[16,22] or both.[28]

A main strength of the study is that around 90% of subjects had occupational data. In addition, over 90% of interviews in cases and controls were performed directly with the patient. These figures are seldom achieved in pancreatic cancer, and are a consequence of the prompt identification of cases with putative diagnoses.

The diversity of occupations assessed may raise two concerns. First, in some occupations the number of exposed cases was low, which yielded some imprecise estimates and precluded examination of exposures related to the aluminium industry[35,36] and dry cleaning.[9] It was also impracticable to explore interactions among occupations and lifestyle factors. Interactions may be particularly relevant for occupational compounds with a potential to act as tumour promoters.[43,46] The second concern is multiple testing. To minimize this, our analyses were closely linked to substantive hypotheses and results from previous studies.

This report stems from the first study investigating the role of occupation in pancreatic cancer in Spain. The observed associations are in accordance with results from previous studies. In spite of the study limitations, the increases in risk observed in agricultural and textile workers in women, and for men working in the manufacture of dyes and pigments may deserve further attention.

Acknowledgements

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